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ORIGINAL ARTICLE

Simulation model to estimate the burden of disease due to hepatitis E virus in Dutch pig meat and cost-effectiveness of control measures

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Abstract

Hepatitis E virus (HEV) can lead to liver disease in humans. In the Netherlands, the consumption of pig meat is thought to be the main contributor to the total burden of disease caused by HEV. In this study, the number of cases and lost disability-adjusted-life-years (DALYs) due to HEV in pig meat were estimated by simulating HEV through the pig supply chain, including the farm, transport, lairage, slaughtering, processing, and consumption stages. The first four stages were modeled using a susceptible-exposed-infected-recovered (SEIR) model. For the last two stages, pig meat and liver products were divided into six product categories commonly consumed by Dutch consumers. Depending on the product category, different ways of heating and storing, leading to the reduction of infectious HEV genome copies, were assumed. Furthermore, the model was challenged by four selected control options at the pig farm: the cleaning of driving boards, the use of predatory flies, the use of rubber mats, and the vaccination of finishing pigs. Finally, the cost-effectiveness of these control measures was estimated by estimating the costs per avoided DALY. For the baseline situation, it was estimated that HEV in pig meat would lead to 70 cases and 21 DALYs per year. All control measures led to a decreased number of DALYs, with vaccination leading to the largest decrease: five DALYs per year. However, the costs per avoided DALY ranged from €0.5 to €7.5 million, making none of the control measures cost-effective unless the control measures are also effective against other pathogens.

KEYWORDS
burden of disease, control measures, economics, food safety, zoonoses

1 | INTRODUCTION

Hepatitis E virus (HEV) can cause, like other hepatitis viruses, liver disease in humans that is mostly self-limiting with symptoms such as fatigue, nausea, and fever and in general does not progress to chronicity (Bouwknegt et al., 2007; EFSA, 2017). However, severe HEV infections have been reported in immunosuppressed adults and pregnant women (Al-Shimari et al., 2023; EFSA, 2017). There are four main human HEV types: genotypes 1, 2, 3, and 4 (HEV-1, 2, 3, and 4). The genotype contributes to the pathogenesis of HEV-associated hepatitis. HEV-1 and HEV-2 mainly lead to self-limiting hepatitis in adults. HEV-1 can potentially lead to fatal hepatitis in pregnant women. HEV infection with HEV-3 can become chronic in elderly or immunocompromised patients. HEV infection HEV-4 sporadically leads to chronic infections (Lin & Zhang, 2021). HEV-1 and HEV-2 have been isolated in human outbreaks in low-income countries, whereas HEV-3 and HEV-4 have been isolated in humans, wildlife, and farmed animals in low- and high-income coun-

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tries, with HEV-3 mainly in Europe and HEV-4 mainly in Asia (EFSA, 2017). HEV-3 is the most relevant in pig husbandry in the Netherlands. Therefore, the remainder of this paper focuses on HEV-3. The incidence of HEV-3 infections increased between 2005 and 2015 in the European Union, with 514 cases reported in 2005 and 5617 cases in 2015 (ECDC, 2017). HEV cases lead to disability-adjusted-life-years (DALYs). DALYs are used to estimate the burden of disease of foodborne illnesses. DALYs are the sum of years of life lost due to premature mortality and the years lived with disability. One DALY represents 1 year of healthy life lost. In the Netherlands, a considerable number of DALYs due to HEV were attributed to the food in the Netherlands: 70, 71, 63, 54, and 43 DALYs in 2017, 2018, 2019, 2020, and 2021, respectively (Benincà et al., 2022). In 2021, 32 out of the 43 HEV-related DALYs attributed to food were attributed to pig meat (Benincà et al., 2022). Therefore, pigs are thought to be the main reservoir of HEV, and the consumption of pig meat is a major source of infection for humans.

Infectious viral particles are mainly found in the blood and liver of pigs (EFSA, 2017). In the Netherlands, HEV RNA was detected in 12.7% of liver samples, 70.7% of liverwurst samples, and 68.9% of liver pâté samples from Dutch retail stores (Boxman et al., 2019). HEV RNA was not detected in pork chops or fresh sausages (Boxman et al., 2019). However, HEV RNA has been found in 33 out of 36 batches of nonheated samples of porcine blood (Boxman et al., 2017). Blood can either be an ingredient in meat products or a residual amount can be left in the meat after bleeding (Crotta et al., 2021) and could potentially lead to a small amount of HEV RNA in pork chops or sausages (Bouwknegt et al., 2009; Pavio et al., 2017; Salines, Demange, et al., 2019; Williams et al., 2001).

HEV infections start at the pig farm but cross-contaminates at the slaughterhouse and improper processing or heating of pig meat before consumption are important for the probability of human infection. Modeling HEV along the pig supply chain can help risk managers to detect risk factors and assess potential control measures. So far, models have been developed for different parts of the pig supply chain of which transmission of HEV between pigs on a farm is the most described and modeled transmission route. For example, Andraud et al. (2013) presented a model to describe three main transmission routes within a pig farm: via direct contact between pigs, feces within pens on a farm, and feces between pens on a farm. Crotta et al. (2018) presented a model describing the transmission of HEV on a pig farm, with as an outcome the proportion of animals with contaminated liver and gall bladder and the proportion of animals carrying HEV in intestines at the slaughter stage. The model by Salines, Dumarest, et al. (2019) described HEV infection patterns between pigs on pig farms and assessed the impact of immunomodulating coinfections such as porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2) on the risk of HEV infection. Transmission between pig farms is another pathway, which may occur when a farm buys infected piglets or pigs from another farm or via livestock transportation vehicles that visit different farms (Nantel-Fortier et al., 2016). A model was developed to assess the HEV transmission and persistence patterns in the pig production sector in France, considering both within-farm dynamics and animal movements based on actual data (Salines et al., 2020). At the slaughtering stage, Crotta et al. (2021) modeled HEV transmission during the slaughtering of pigs and evaluated the risk of HEV being present on pig carcasses and in meat at the end of the slaughtering process. Furthermore, cross-contamination at the slaughterhouse and the meat processing plant appears to be possible via hands, gloves, and working surface (Pavio et al., 2017). Several exposure models have been developed to estimate the risk of human HEV infection caused by food and pig meat consumption. The estimated exposure to HEV through the consumption of contaminated food, as well as the burden of disease of HEV in Switzerland (Müller et al., 2017; Sarno et al., 2017) and in four other European countries (Germany, the United Kingdom, France, and the Netherlands) (Ji et al., 2021), has been previously modeled. Furthermore, Yang et al. (2021) recently presented a multihost and multiroute transmission dynamic model to estimate the risk of human HEV infections through pig meat and contact with contaminated humans.

However, a model simulating the spread of HEV through the pig supply chain from farm to fork, including the farm, transport, lairage, slaughtering, processing, and consumption stages that can easily be challenged by different types of control measures at different stages of the chain, is currently lacking. This research aimed to fill this knowledge gap by first creating a farm-to-fork simulation model to estimate the expected number of cases and DALYs due to the consumption of pig meat contaminated with HEV and, second, by challenging the model with several types of control measures at farm level and to estimate their cost-effectiveness.

2 | MATERIALS AND METHODS

2.1 | Conceptual model

Our conceptual model is depicted in Figure 1. Our model consists of several stages: (1) the farm stage, (2) the transport stage, (3) the lairage stage, (4) the slaughtering stage, (5) the processing stage, and (6) the consumption stage. The developed susceptible-exposed-infected-recovered (SEIR) model for the first four stages is described in Sections 2.2–2.4. This model is based on a previously derived susceptible-infected-recovered (SIR) model for *Salmonella* spp. (van der Gaag, Vos, et al., 2004). The time step of our model is a day, following the model of van der Gaag, Vos, et al. (2004). Processing and consumption were included as described in Sections 2.5 and 2.6, respectively. The number of expected DALYs per year due to HEV in pig meat in the Netherlands was estimated as described in Section 2.7. Several control measures were selected, focusing on the farm stage since this stage is the most important stage regarding the spread of HEV (Section 2.8), and their costs and effectiveness were estimated (Section 2.9). The statistical software R, version 4.1.0 (R

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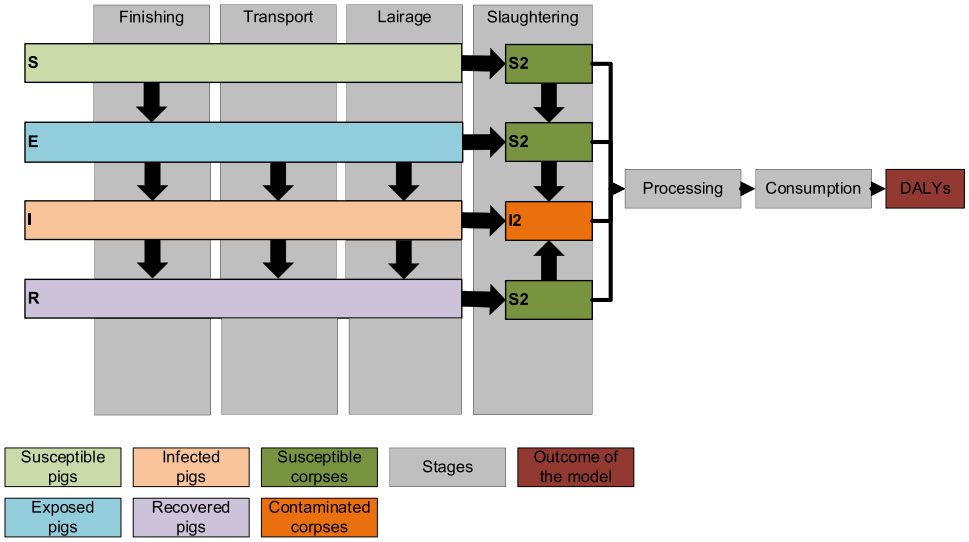

FIGURE 1 Conceptual farm-to-fork model for HEV in the Dutch pig supply chain.

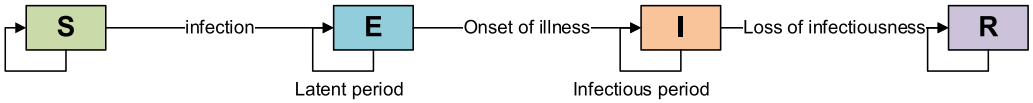

FIGURE 2 States at the farm stage.

Core Team, 2021), with the packages "mc2d" (Pouillot, 2010) and "deSolve" (Soetaert et al., 2010) was used to run the model. The stochastic model consisted of 10,000 iterations to account for uncertainties.

2.2 | The farm stage

The farm stage model represents a pig farm comprising 10 pens with 100 pigs (N_{pen}) in each pen. The number of days a pen stays at the farm before going to the slaughterhouse was assumed to be 182 days (26 weeks). After the fattening period, the farm sells the pen to a slaughterhouse. At the pig farm, pigs can be in one of the four states: susceptible (S), exposed (E), infected (I), and recovered (R). Susceptible animals are HEV-free animals with a negative serology. Exposed animals have been exposed to HEV but are not infectious yet. Infected animals are infectious and excrete HEV RNA via their feces. Recovered animals are not infectious anymore, have a positive serology, and are protected from another HEV infection. The different states are depicted in Figure 2.

Every state in the SEIR model has a certain probability that an animal remains in the same state or moves to another state. When the piglet is born, the first time step of the model, a piglet starts in state S. The transition probabilities are modeled with the following differential equations that are based on van der Gaag, Vos, et al. (2004) and Ji et al. (2021):

$$\frac{dS}{dt} = -\left[\left(\beta_d + \beta_e\right) * S * I + \beta_i * S\right], \tag{1}$$

$$\frac{dE}{dt} = [(\beta_d + \beta_e) * S * I + \beta_i * S] - \frac{1}{\delta} * E, \tag{2}$$

$$\frac{dI}{dt} = \frac{1}{\delta} * E - \frac{1}{\gamma} * I, \tag{3}$$

$$\frac{dR}{dt} = \frac{1}{\gamma} * I. \tag{4}$$

With β_d the direct transmission rate between pigs in the same pen, the β_e transmission rate due to external causes such as wildlife, rodents, or people, β_i the indirect transmission rate between pens via the oral-fecal route, δ the latent period, γ the infectious period, S, E, I, R the number of susceptible, exposed, infected, and recovered pigs within a pen, respectively.

$$\beta_d = \beta_{d0}\left(1 - e^{-0.06t}\right), \tag{5}$$

$$\beta_e = \beta_{e0}\left(1 - e^{-0.06t}\right), \tag{6}$$

$$\beta_i = \beta_{i0}\left(1 - e^{-0.06t}\right), \tag{7}$$

$$\beta_{i0} = f_p * r_p * D * cor. \tag{8}$$

where β_d, β_e, and β_i are time-dependent as described in Equations (5)–(7). During the first weeks, piglets are protected

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TABLE 1 Inputs for the farm stage of the model.

Input	Description	Value	Reference
B_{d0}	Direct transmission rate within a pen	0.15	0.13 [95% CI 0.092 – 0.14] (Backer et al., 2012; Bouwknegt et al., 2008) 0.15 [95% CI 0.03 – 0.31] (Andraud et al., 2013) 0.16 (Ji et al., 2021)
B_{e0}	The probability of being infected by external causes	0.015	Assumption: 1% of the transmission rate within pens comes from external sources
δ	Latent period (days)	Pert (minimum = 7, mode = 12, maximum = 17)	9; 17 (Bouwknegt et al., 2008) 13 [95% CI 9 – 17] (Salines et al., 2015) 7 [95% CI 3 – 12] (Andraud et al., 2013) 6 (Ji et al., 2021)
γ	Infectious period (fecal shedding) in days	Pert (minimum = 11, mode = 27, maximum = 141)	24 [95% CI 18 – 33] (Backer et al., 2012) 27 [97% CI 20 – 39] (Backer et al., 2012) 49 [95% CI 17 – 141] (Bouwknegt et al., 2008) 13 [95% CI 11 – 17] (Bouwknegt et al., 2008; Meester et al., 2021) 23 [95% CI 19 – 28] (Bouwknegt et al., 2009)
f_p	Fraction of pens with infectious pigs	0.68 * 0.1	HEV IgG was detected in the sera of 67.7% of pigs (Boxman et al., 2022). Assumption: 68% of farms have infectious pigs. Assumption: 10% pens have infectious pens on a farm with infectious pigs
r_p	the probability of pig infection per HEV particle infected	$1.3*10^{-9}$	Ji et al. (2021)
D	the amount of HEV gc per gram feces (from infectious pigs in nearby pens)	Pert (minimum = 10^3, mode = $10^{4.6}$, maximum = $10^{8.2}$)	Boxman et al. (2022)
cor	Correction factor	10^{-2}	Bouwknegt et al. (2011)

Abbreviations: HEV, hepatitis E virus; IgG, immunoglobulin G.

with maternal immunity, which decreases over time. β_{d0}, β_{i0}, and β_{e0} are the direct transmission rate between pigs in the same pen, the indirect transmission rate between pens via the oral-fecal route, and the transmission rate due to external causes, after loss of maternal immunity, respectively. β_{i0} is estimated using *fp* the fraction of pens with infectious pigs within a farm, *rp* the probability of pig infection per infectious HEV particle, *D* the amount of HEV gc per gram feces (from infectious pigs in nearby pens), and *cor* a correction factor as described in Equation (8). The values for these inputs are derived from the literature and are listed in Table 1.

2.3 | The transport and lairage stages

When pigs are ready for slaughter, they are transported to the slaughterhouse. There they are kept in lairage to reduce stress levels as this negatively affects the meat quality as well as improves animal welfare. Both stages are assumed to last for 1 day, the smallest time step in our model, similar to Mu et al. (2024). The transitions between the susceptible and exposed states are modeled with the following equations:

$$\frac{dS}{dt} = -\beta_{d0} * S * I, \tag{9}$$

$$\frac{dE}{dt} = \beta_{d0} * S * I - \frac{1}{\delta} * E. \tag{10}$$

With β_{d0} the direct transmission rate between pigs in the same pen after loss of maternal immunity, *S*, *E*, and *I* the number of susceptible, exposed, and infected pigs within a pen, respectively. The transitions between the exposed, infected, and recovered states follow the same rules as during the farm stage (Equations 7 and 8).

2.4 | The slaughtering stage

At the time of slaughtering, the pig corpse (i.e., carcass with organs) harbors HEV (state I2) in case it originates from pigs with a recent infection (state I). Pig corpses in state I2 remain in state I2 during the entire slaughtering stage. These corpses contain HEV RNA, referred to as genome copies (gc) in at least the cecum. Corpses from pigs slaughtered in states S, E, or R move to state S2 at the start of the slaughtering stage. Corpses in state S2 are at risk of contamination via cross-contamination. The slaughtering stage is modeled following a previously developed model for *Salmonella* spp. (Mu et al., 2024). Cross-contamination could theoretically happen via fecal or biliary cross-contamination during evisceration via the equipment used. Cross-contamination could theoretically happen via fecal or biliary cross-contamination during evisceration via the equipment used. The events influencing the likelihood of this pathway are the likelihood that HEV is present in feces and/or bile, the likelihood of rupturing organs during evisceration, the amount of feces and/or

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TABLE 2 Inputs for the slaughtering stage of the model.

Input	Description	Value	Reference
$cross_{min}$	Minimum value for cross-contamination	0.00001	Assumption
			1% of the value used in Mu et al. (2024)
$cross_{max}$	Maximum value for cross-contamination	0.0025	Assumption
			1% of the value used in Mu et al. (2024)
Q_{down}	Relative percentage $cross_{min}$ and $cross_{max}$ will decrease after a noncontaminated corpse passed the slaughter line	0.05	Mu et al. (2024)
Q_{up}	Relative percentage $cross_{min}$ and $cross_{max}$ will increase after a contaminated corpse passed the slaughter line	0.1	Mu et al. (2024)

bile leak, the level of HEV contamination in feces and bile, and the proportion of nonvisible contamination remaining on the carcass (Crotta et al., 2021). Following the models of van der Gaag, Vos, et al. (2004) and Mu et al. (2024), cross-contamination via equipment was modeled with $cross_{min}$ and $cross_{max}$ which are the minimum and maximum values for cross-contamination. These values decrease with a factor Q_{down} when a clean corpse passes the slaughter line and increase with a factor Q_{up} when a contaminated corpse passes the slaughter line. However, the probability of cross-contamination for HEV is very low and a limited number of gc can possibly be transmitted (Crotta et al., 2021). Therefore, we assumed the values for $cross_{min}$ and $cross_{max}$ were equal to 0.1% of the values used in the model of Mu et al. (2024).

The following equations were used:

$$\frac{dS2}{dt} = -\left[(uniform\,(cross_{min}; cross_{max}) * Q_{up} * I2 + \left(uniform\,(cross_{min}; cross_{max}) * Q_{down} * S2\right]/2, \tag{11}$$

$$\frac{dI2}{dt} = \left[(uniform\,(cross_{min}; cross_{max}) * Q_{up} * I2 + \left(uniform\,(cross_{min}; cross_{max}) * Q_{down} * S2\right]/2. \tag{12}$$

The inputs are detailed in Table 2. After the slaughtering stage, corpses can either be contaminated (state I2) or noncontaminated (state S2) (Figure 1).

2.5 | Processing

For the processing stage, six different product categories were chosen, regularly consumed by Dutch consumers (Table 3). The first three product categories consisted of products bought raw from the market and to be cooked at home: (1) pig meat, for example, spare rib, tenderloin, fillet, fricandeau, gammon, bacon, schnitzel, and stewing meat; (2) sausages and minced meat; and (3) pig liver. The last three categories are ready-to-eat (RTE) products consumed with bread or as a snack; (4) RTE cold pig meat, for example, cooked or grilled sausages, heated at the industry level; (5) RTE dried pig sausages such as salami or chorizo, consumed unheated; and (6) RTE liver products such as live pâté or liver sausage.

At the end of the slaughtering stage, corpses in state I2 possibly lead to pig meat and liver products containing HEV gc. Since most corpses in state I2 come from infectious pigs carrying HEV in their feces, we applied the conversion rates ω_{serum} and ω_{liver} to estimate the percentage of corpses in state I2 positive for HEV gc in the blood and liver, respectively. We assumed that for product categories 1, 2, 4, and 5, the pig meat products were contaminated due to the residual blood in these products. Product categories 3 and 6, pig liver products, were contaminated due to HEV-positive livers.

The number of gc in HEV-positive products was based on previous studies and is listed in Table 3. Infectious HEV particles can be inactivated by properly heating pig meat and liver products before consumption. Heating at temperatures above 71°C reduces the HEV titers significantly (Barnaud et al., 2012; Stunnenberg et al., 2023). We assumed that some products, or a fraction of some products were not heated up to 71°C but instead cooked medium at 55°C, leading to less reductions (Evers et al., 2017; Stunnenberg et al., 2023). Storage can also reduce infectious particles (Stunnenberg et al., 2023). The processing steps leading to HEV inactivation are product category dependent. The log reductions of infectious HEV particles based on different ways of processing are based on the study of Stunnenberg et al. (2023) and are listed in Table 3.

2.6 | Consumption

The consumption of the six different product categories described in the previous section was derived from the Dutch National Food Consumption Survey (VCP) data collected from 2019 to 2021 (RIVM, 2023). All products with pig meat or liver as the main ingredient were considered. We used the Dutch Food Composition Database (NEVO), which consists of more than 2300 foods defined by a unique combination

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TABLE 3 Inputs for the number of infectious particles per pig meat or liver product.

Product category	Conversion state I to blood/liver positive	Genome copies in positive samples at market level (gc HEV / g)	Processing steps that can possibly inactive HEV	Log_{10} reduction infectious HEV RNA[a]	Percentage reduction (%)[b]
1. Pig meat to be prepared (spare rib, tenderloin, fillet, fricandeau, gammon, loin chop, bacon, schnitzel, stewing meat, shoarma, etc.)	$\omega_{serum} = 0.271$[c]	Blood: 1100[d] Residual blood = Uniform(2;9)*10^{-3} mL/g[e]	At consumer level: Ham, tenderloin,[f] cooked medium,[a,g] remaining products heated to at least 71°C	Medium: [0.52–1.31] >71°C: 3.69	[69.80–95.10] 99.98
2. Sausages and minced meat to be prepared (pig sausages, smoked sausages, blood sausages, minced meat, etc.)	$\omega_{serum} = 0.271$[c]	170[d]	At the consumer level: minced meat and sausages, 2.3% and 13.9% are cooked medium, respectively [f,g,h,] Rest: Heated to at least 71°C	Medium: [0.52–1.31] >71°C: 3.69	[69.80–95.10] 99.98
3. Pig liver to be prepared	$\omega_{liver} = 0.254$ [c]	6705 [i]	At the consumer level: heated to at least 71°C	>71°C: 3.69	99.98
4. RTE cold pig meat used on bread or as a snack (cooked sausages, grilled sausages, etc.)	$\omega_{serum} = 0.271$ [c]	170 [d]	At industry level: Heated to at least 71°C	>71°C: 3.69	99.98
5. RTE dried pig sausages used on bread or as a snack (salami, chorizo, other dried sausages)	$\omega_{serum} = 0.271$ [c]	116[j]	At consumer level: Stored between 0 – 4 weeks at a temperature between 4 and 21°C	Storage: [0.00–2.35]	[0.00–99.55]
6. RTE liver products used on bread or as a snack (liver pate, liver sausage, etc.)	$\omega_{liver} = 0.254$ [c]	1702 [k]	At the consumer level (10% of products): cooked medium[g] At industry level (90% of products): heated to at least 71°C Stored for 0–1 week at a temperature between 4 and 10°C	Medium: [0.52–1.31] > 71°C: 3.69 Storage: [0.00–0.63][l]	[69.80–95.10] 99.98

Abbreviations: HEV, hepatitis E virus; RTE, ready to eat.
[a]Stunnenberg et al. (2023).
[b]$P = (1 - 10^{-L}) * 100$, with P the percent reduction and L the log reduction.
[c]Out of 59 cecum-positive pigs, 16 are serum-positive and 15 liver positive (Boxman et al., 2022).
[d]Boxman et al. (2017).
[e]Crotta et al. (2021).
[f]Ham, tenderloin accounts for 24% of the products in category 1, minced meat accounts for 64% in product category 2, and sausages account for 36% in product category 2 (based on the VCP consumption data; RIVM, 2023).
[g]Assumption: medium: 55°C for 5–10 min.
[h]Evers et al. (2017).
[i]Boxman et al. (2017), gc is for the unheated product.
[j]Boxman et al. (2020), geometric mean, gc as found on the Dutch market.
[k]Boxman et al. (2019), geometric mean, gc as found on the Dutch market.
[l]Assumption that the inactivation factor during storage is similar to the matrix "dried sausage".

of, among others, energy, protein, carbohydrate, fat and fatty acids, vitamins, and minerals. This unique combination, the NEVO code, was used to aggregate the VCP data for all participants in order to derive the number of grams consumed per consumer per year for each product category that can be found in the NEVO database (Table 4). The percentages of pig meat and liver in each product were considered. For example, for mixed-meat meatballs that are made from both beef and pig meat, only 50% of the product was included as pig meat. The portion sizes of 65 g for product categories 1 and 2 and 30 g for product categories 3, 4, 5, and 6 were assumed, based on the VCP data (Table 4).

2.7 | Estimation of the burden of disease

The results of all previous stages: the farm, transport, lairage, slaughtering, processing, and consumption are needed to estimate the burden of disease in terms of expected DALYs per year in the Netherlands. The number of HEV cases expected

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TABLE 4 Inputs for the consumption stage of the model.

Product category	Consumption (g/year)[a]	Product category[a]
1. Pig meat to be prepared	4,592	65
2. Sausages and minced meat to be prepared	3,530	65
3. Pig liver to be prepared	230	30
4. RTE pig used on bread or as a snack	2,079	30
5. RTE raw pig sausages used on bread or as a snack	824	30
6. RTE liver products used on bread or as a snack	933	30

Abbreviation: RTE, ready to eat.
[a]Derived from RIVM (2023).

TABLE 5 Inputs to estimate the human health burden due to the consumption of pig meat in the Netherlands.

Input parameter	Description	Value, reference
$C_{ccontam}$	Percentage of contaminated corpses	Output SEIR model: 95% confidence interval
ω_i	Conversion rate from cecum positive to serum or liver positive	Table 3
GC_i	Number of genome copies per portion per food category	Table 3
R_{treat_i}	Reduction in HEV genome copies	Table 3
$N_{consumption\_i}$	Consumption in g/person/year	Table 4
PS_i	Portion size	Table 4
N_{NL}	Number of consumers in the Netherlands	17,475,415 (CBS, 2021)
Ser_{NL}	Percentage of the Dutch population having a positive serology for HEV (not susceptible to infection)	29% (van Gageldonk-Lafeber et al., 2017)
P_{human}	the probability of human infection per HEV genome copies ingested	$2.5*10^{-9}$ (95% CI $6.8*10^{-10}$ – $1.5*10^{-8}$) (Ji et al., 2021)

Abbreviations: HEV, hepatitis E virus; SEIR, susceptible-exposed-infected-recovered.

due to the consumption of contaminated pig meat and liver products was estimated using the following equation:

$$\sum_{i=1}^{6} C_{infected} * \omega_i * GC_i * \left(\frac{N_{consumption_i}}{PS_i} * N_{NL}\right) * \left(1 - R_{treat_i}\right) * P_{human} * (1 - Ser_{NL}). \quad (13)$$

With i the six different product categories, C_{contam} is the percentage of contaminated corpses (in state I2 at the end of the slaughtering stage: the output from the previously described SEIR model), ω_i is the conversion rate from cecum positive to blood or liver positive, GC_i is the number of gc per portion without taking processing into account, $N_{consumption\_i}$ is the consumption per product category in the Netherlands in g/person/year, PS_i is the portion size depending on the product category, N_{NL} is the number of consumers in the Netherlands, R_{treat_i} is the reduction of HEV gc during processing, P_{human} is the probability of human infection per infectious HEV gc ingested, and Ser_{NL} is the percentage of Dutch consumers that already have a positive serology for HEV. The values used as input are listed in Table 5.

DALYs were estimated based on the number of expected DALY per expected case as estimated by Benincà et al. (2022). Benincà et al. (2022) estimated between 0.3 and 0.4 DALYs per case with a discounting rate of 0% and 1.5%, respectively, with the latter value representing the situation in case years of life lost in the present are valued more than years of life lost in the future.

2.8 | Control measures: Effectiveness

HEV is mostly transmitted during the farm stage. Therefore, control measures are studied at this stage. Selected control measures had to comply with the following three criteria: (1) they should be applicable to pig husbandry in the Netherlands, (2) they must have been proven to be effective, and (3) secondary data about their effectiveness should be available in the literature. Control measures mentioned in the studies of Meester et al. (2023) and Ji et al. (2021) complied with these criteria. The study of Meester et al. (2023) measured the effectiveness of four control measures based on data from Dutch pig farms: driving boards cleaned weekly or after every pig contact, fly control with predatory flies, rubber mats on solid floors in fattening pens, and steel slatted floor in fattening pens. Based on the data provided, a relative risk for each control measure was estimated. Based on a case-control study with 215 farms that delivered to three Dutch slaughterhouses, with repeated cross-sectional sampling of pigs from pens of pigs delivered to the slaughterhouse by Meester et al. (2023), cleaning driving boards, predatory flies, and rubber mats on the floor lead to a decrease of 17%, 21%, 27% of the

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TABLE 6 Costs of the four selected control measures, with the costs of pigs at the national level.

Control measure	Costs (€/pig/year)	Farms without measure (%)[a]	Estimated finishing pigs without measure (million)[b]	Estimated implementation cost for the Netherlands (million €/year)	Effect	Direct transmission rate [c]
Vaccination	7.26	100	5.16	37.44	36% lower risk of HEV infection at the start of the slaughtering stage (Ji et al., 2021)	0.070
Weekly cleaning of driving boards	0.39	52	2.68	1.04	17–18% lower risk of HEV infection at the start of the slaughtering stage (univariate analysis) (Meester et al., 2023)	0.083
Predatory flies	2.31	59	3.06	7.08	21% lower risk of HEV infection at the start of the slaughtering stage (univariate analysis) (Meester et al., 2023)	0.079
Rubber mats on the floor	2.25	82	4.22	9.50	27% lower risk of HEV infection at the start of the slaughtering stage (univariate analysis) (Meester et al., 2023)	0.075

Abbreviation: HEV, hepatitis E virus.

[a]Vaccination: no vaccine is available yet, so no farms have yet implemented. The other control measures are based on data from Meester et al. (2023): 38 out of 73 farms without weekly cleaning driving boards; 19 out of 32 farms without predatory flies; 59 out of 72 farms without rubber mats on the floor.

[b]Assuming that the farms in Meester et al. (2023) are representative of the entire finishing pig farm population in the Netherlands and that the implementation rate of each measure is independent of farm size. In 2022, the number of finishing pigs in the Netherlands was 5.16 million (Agrimatie, 2023a).

[c]Based on Figure 4, rounded to three decimals.

prevalence of HEV infectious pigs at the start of the slaughtering stage. The last control measure of steel slatted floor was found to have a very low relative risk reduction and was therefore excluded from further analysis in our study. The study of Ji et al. (2021) theoretically estimated the effectiveness of pig vaccination against HEV in several European countries, including the Netherlands. Although currently no vaccine is on the market yet, several vaccines are in development so these might become available soon. Vaccination would lead to a decrease of 36% in the prevalence of infectious pigs at the start of the slaughtering stage according to Ji et al. (2021). Thus, four control measures at the finishing stage were included in our study: weekly cleaning of driving boards, fly control with predatory flies, rubber mats on solid floors in fattening pens, and vaccination.

The assumption was made that these control measures affect the transmission rate within a farm. We estimated how much the transmission rate within a farm would need to be decreased to achieve the calculated relative risk.

Potential additional benefits can only be realized for farms that have not yet implemented the control measures selected. A HEV vaccine for pigs is not yet commercially available, so the adoption rate of vaccination (i.e., the current application) is zero. For the other three control measures, Meester et al. (2023) provided adoption rates in their sample, which can be found in Table 6.

2.9 | Control measures: Costs

Incurred control measure costs were calculated per finishing pig per year. The cost of weekly cleaning of all driving boards consisted of costs of water and labor of the pig farmer (three minutes per board per cleaning). The costs of predatory flies consisted of the costs of boxes with pupae and pig farmer labor for hanging the boxes four times a year. Costs of rubber mats consisted of depreciation, interest, and maintenance costs of the investment. The costs of labor of the pig farmer to install the mats were accounted for as an investment (van Wagenberg & van Horne, 2016). Costs of vaccination consisted of costs of the vaccine and labor to administer the vaccine. Pigs were assumed to be vaccinated twice at 10 and 12 weeks (Go et al., 2021; Ji et al., 2021). A pig farmer was assumed to administer the vaccine together with an employee at a rate of 400 doses per hour. Detailed economic input data of the control measures are presented in Appendix A.

To extrapolate the additional costs of the control measures from the farm level to the national level, we needed to account for current adoption levels. Assuming that the sample provided by Meester et al. (2023) is representative of the finishing pig farm population in the Netherlands and the adoption rate of each control measure is independent of farm size, the number of finishing pigs, not yet subject to each control measure, was estimated by multiplying the percentage of farms on which each intervention was not yet implemented by the number of finishing pigs in the Netherlands in 2022. Annual national costs were estimated by multiplying the number of finishing pigs not yet subject to each control measure by the control measure costs per finishing pig per year.

The cost-effectiveness of the control measures was measured with the cost-effectiveness ratio (CER). The CER of an intervention was the estimated national costs of the intervention divided by the estimated national public health benefits due to the intervention and was expressed in euros per avoided DALY.

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2.10 | Fraction of pig meat consumed in the Netherlands from domestically raised finishing pigs

The control measures only have an effect on pig meat produced in the Netherlands. Therefore, the fraction of pig meat consumed in the Netherlands from domestically raised finishing pigs was estimated. The Dutch pig sector is an open market with considerable import and export of both live finishing pigs and pig meat. HEV control measures implemented on finishing pig farms in the Netherlands would reduce the health risks of consumers in the Netherlands and other countries where the meat of these finishing pigs is consumed. However, if measures would be implemented in the Netherlands only, the meat consumed by Dutch consumers not stemming from domestically raised finishing pigs would not offer additional health protection to Dutch consumers. This needs to be considered when estimating the public health gains in the Netherlands due to HEV control measures implemented on Dutch finishing pig farms. Because most of the imported pig meat originates from Germany and Belgium (Wisman & Jukema, 2017) with quite similar production systems to those in the Netherlands, the risk factors and infection levels without intervention were assumed to be similar for both domestically produced and imported pig meat.

To estimate the fraction of pig meat consumed in the Netherlands from domestically raised finishing pigs, we used a certification approach, because the default method to account for trade characteristics as proposed by Mangen et al. (2007) was found not to be sufficiently reliable anymore. For 2022, that default method would result in a fraction of 0.32 (see Appendix B), which is unrealistically low. Therefore, we diverted to using the amount of pig meat certified according to the Dutch "Beter Leven" certification scheme focusing on improved animal welfare, which specifically produces for Dutch supermarkets (Dierenbescherming, 2023). In 2022, approximately 60% of fresh pig meat and 80% of pig meat cold cuts sold in the Netherlands to consumers were sold in supermarkets (Agrimatie, 2023b). Logatcheva and Herceglić (2023) indicated that "almost all" of this fresh meat (we assumed 99%) and a "high fraction" of these cold cuts (we assumed 80%) were "Beter Leven" certified. Thus, between 60% (= 99% * 60%) and 64% (= 80% * 80%) of the pig meat purchased in the Netherlands was "Beter Leven" certified and from domestically raised pigs. In addition, pig meat was sold through food service and specialty shops. Approximately 26% of the meat sales were in food service and 1% in specialty shops. Approximately 7% of those sales in food service and 100% of those in specialty shops were produced under a sustainability label (Logatcheva & Herceglić, 2023). Assuming that these percentages are representative of pig meat and that pig meat with these sustainability labels came from finishing pigs raised in the Netherlands, another 3% (= 26% * 7% + 100% * 1%) of the pig meat sold in the Netherlands was of domestic origin. Thus, we estimated that in 2022, a fraction of approximately 0.65 of the pig meat sold in the Netherlands came from domestically raised finishing pigs.

2.11 | Sensitivity analysis

The sensitivity of the model to changes in input parameters was assessed by decreasing and increasing the major input parameters by 50%. Major input parameters considered comprised the latent period, the infectious period, the pen size, the number of infectious particles present in the different products, the conversion rates from cecum positive to serum or liver, and the effect of heating. Furthermore, we raised the fraction of pig meat originating from the Netherlands to 0.80 and 0.90 in a sensitivity analysis as the estimated fraction of 0.65 is a lower bound value.

3 | RESULTS

3.1 | Baseline results

The spread of HEV in a pig pen is shown in Figure 3. From approximately 50 days onwards, maternal immunity is lost, and the disease starts to spread. On average, considering all the baseline assumptions described above, the model predicts that 26.2% (95% CI [25.9–26.4]) of pigs at the end of the farming stage are infected and infectious, excreting HEV in the feces. The percentage of pigs being infected or having been infected and recovered during their lifetime is much higher with 68% on average for the baseline scenario (Figure 3). The estimated fraction of contaminated corpses according to our model is on average 25.9 (95% CI [25.6–26.1]) (Table 7), slightly lower than the estimated percentage at the end of the farming stage since pigs can still recover during transport and lairage. Applying the conversation rates (Table 3) leads to a calculated 6.6% of livers being HEV positive (Table 7). Furthermore, the model predicts that a total of 70 human cases per year with HEV infections are due to the consumption of pig meat, with 67% (47/70 = 67%) of the cases attributable to dried sausages and 23% (16/70 = 23%) attributable to RTE liver products (Table 7). These 70 cases would result in 21 DALYs per year without discounting.

3.2 | Control measures

Based on our model, Figure 4 shows the prevalence of infectious pigs at the start of the slaughtering stage depending on the transmission rate within a farm. Based on Figure 4, we deduced that the transmission rate within a farm was 0.083, 0.079, 0.075, and 0.070 for the cleaning of driving boards, the use of predatory flies, the use of rubber mats on the floor, and vaccination, respectively.

Table 6 shows that the costs of control measures varied from €0.39 per pig per year for cleaning driving boards to €7.26 per pig per year for vaccination. The costs of predatory flies and rubber mats, both approximately €2.30 per pig per year, are in between the costs for cleaning driving boards and vaccination. Table 6 also provides the total costs of implementing each control measure on all finishing pig farms in

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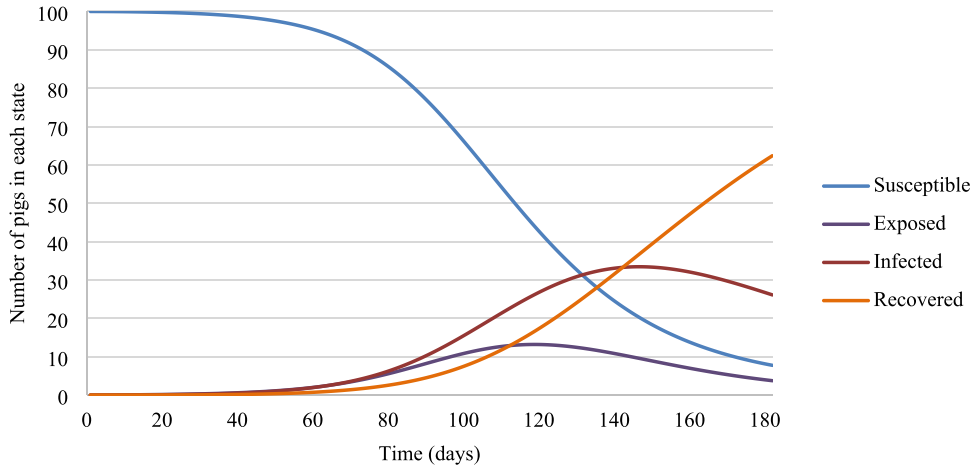

FIGURE 3 States at farm level—following one average pen of 100 pigs (0 – 26 weeks old).

TABLE 7 Results—Estimated human health burden due to HEV in pig meat and liver for one year in the Netherlands.

	Baseline average	Predatory flies	Rubber mats	Cleaning driving boards	Vaccination
HEV Prevalence (%) in cecum at the slaughtering stage (*SD*)	25.9 (12.7)	20.5 (14.4)	18.9 (14.1)	21.8 (14.8)	16.9 (13.5)
HEV prevalence (%) in liver at the slaughtering stage (*SD*)	6.6 (3.2)	5.2 (3.7)	4.8 (3.6)	5.5 (3.8)	4.3 (3.4)
Pig meat to be prepared cases	1	1	1	1	1
Sausages and minced meat to be prepared cases	4	4	4	4	3
Pig liver to be prepared cases	2	1	1	1	1
RTE pig used on bread or as snack cases	0	0	0	0	0
RTE dried pig sausages used on bread or as snack cases	47	40	39	43	36
RTE liver products used on bread or as snack cases	16	14	14	15	13
Total cases (*SD*)	70 (11)	62 (15)	58 (13)	63 (12)	53 (14)
DALY (discounting 0%) (*SD*)	21 (3)	18 (4)	17 (4)	19 (3)	16 (4)
DALY (discounting 1.5%) (*SD*)	28 (4)	24 (5)	23 (5)	25 (5)	21 (6)

Abbreviations: DALY, disability-adjusted-life-years; HEV, hepatitis E virus; RTE, ready to eat; SD, standard deviation.

TABLE 8 Cost-effectiveness of the four selected control measures.

	DALYs avoided per year in the Netherlands	Costs (million €/year)	Costs per avoided DALY (million €)
Predatory flies	3	7.08	2.36
Rubber mats	4	9.50	2.38
Cleaning of driving boards	2	1.04	0.52
Vaccination	5	37.44	7.49

Abbreviation: DALYs, disability-adjusted-life-years.

the Netherlands. Costs of weekly cleaning driving boards are lowest at €1 million per year and of vaccination highest at €37 million per year. The costs of predatory flies and rubber mats were in between €7 and €10 million per year.

Table 7 shows the estimated burden of disease due to HEV in pig meat and liver products in the Netherlands. All control measures led to a decrease in expected illnesses and expected DALYs. Vaccinating finishing pigs led to the largest decrease of, on average, 5 DALYs per year (Table 7). Table 8 shows the CER for the different control measures. The costs per avoided DALY were approximately €0.5 million for the cleaning of driving boards, €2.4 million for the use of predatory flies and the use of rubber mats, and €7.5 million for the vaccination of pigs.

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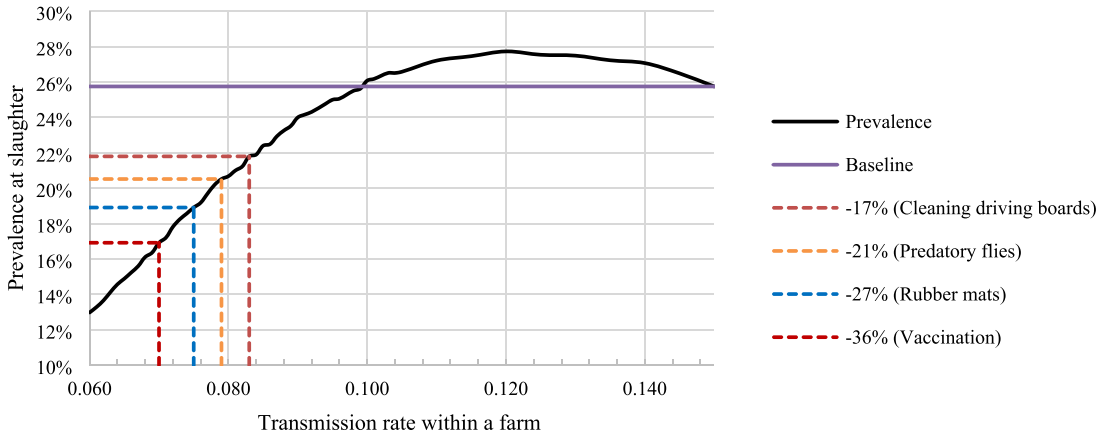

FIGURE 4 Prevalence at the entry of the slaughtering stage as a function of the transmission rate within a farm.

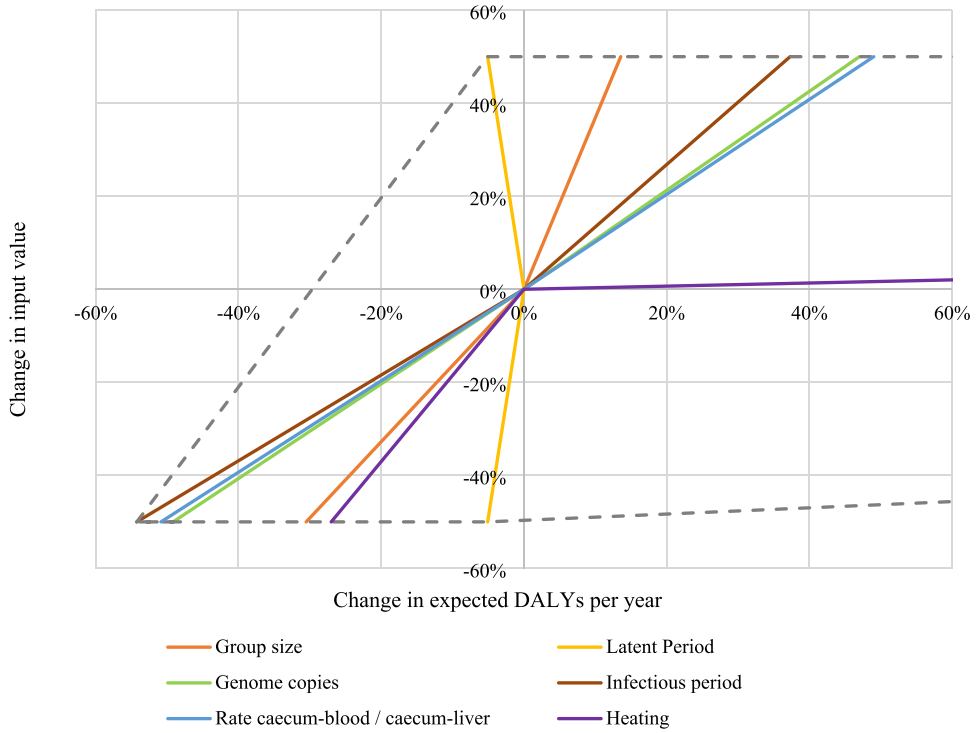

FIGURE 5 Sensitivity analysis—effect of major inputs on the results. DALYs, disability-adjusted-life-years.

3.3 | Sensitivity analysis

At the farm stage, the duration of the infectious period has the largest effect on the results. The latent period has a negligible effect on the results (Figure 5). The pen size has a moderate effect on the results. At the processing stage, the amount of gc per gram product, the cecum–liver or cecum–blood rates, and the effect of heating have the largest effect on the results (Figure 5). Increasing the effect of heating by 50% decreased the number of DALYs expected by 27% (Figure 5). However, decreasing the effect of heating by 50% increased the number of DALYs expected by 1485% (outside the range of Figure 5).

Considering the alternative fraction of pig meat consumed in the Netherlands originating from domestic production of 0.9, the costs per avoided DALY reduced by 20% for the control measure "rubber mats" and by 29% for the control measure "vaccination" (Table 9). In general, the higher consumption in the Netherlands of domestically produced pig meat resulted in higher public health gains and lower costs per avoided case.

4 | DISCUSSION

4.1 | Burden of disease

Our study designed a farm-to-fork simulation model to estimate the expected number of cases and DALYs due to the

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TABLE 9 Sensitivity analysis regarding the percentage of pig meat produced and consumed in the Netherlands.

	DALYs			Costs per avoided DALY (million €)		
	Baseline	80% domestic consumption	90% domestic consumption	Baseline	80% domestic consumption	90% domestic consumption
Predatory flies	18	18	18	2.36	2.36	2.36
Rubber mats	17	17	16	2.38	2.38	1.90
Cleaning of driving boards	19	19	19	0.52	0.52	0.52
Vaccination	16	15	14	7.49	6.24	5.35

Abbreviation: DALY, disability-adjusted-life-years.

consumption of pig meat contaminated with HEV RNA. To the best of our knowledge, this is the first study including the farm, transport, lairage, slaughtering, processing, and consumption stages in one integrated model. Our model estimates 70 human cases per year, equivalent to 21 DALYs. Benincà et al. (2022) estimated that the annual number of DALYs due to pig meat consumption in the Netherlands was between 32 and 53 per year between 2017 and 2021. A possible explanation for this deviation between the two models could first be that the estimation of Benincà et al. (2022) was based on a model build between 2006 and 2009, and the attribution factor was based on two experts consulted in 2008 (Benincà et al., 2022). Much more knowledge about HEV has been gained since then. Another explanation could be that the assumed cecum–liver and cecum–serum conversion rate (Table 3) used in our baseline scenario, which led to an average of 6.6% of pigs with contaminated livers and 7.0% of pigs with contaminated blood, was on the low side. The sensitivity analysis shows that when these rates increased by 50%, our estimation increased from 21 to 32 DALYs per year, within the interval estimated by Benincà et al. (2022). Another possible explanation could be that we did not include any mixing of products in our model. A highly contaminated liver could, for example, contaminate a mix of livers. Boxman et al. (2017) detected HEV RNA in 13% of liver and 70% of liver products in the Dutch market in 2016. In Germany, 15% of pig liver pâté tested positive for HEV RNA (Pallerla et al., 2021) and in Canada 29% of pig liver pâté samples from grocery stores tested positive for HEV (Chatonnat et al., 2023).

Müller et al. (2017) assessed the burden of disease due to HEV in pig liver products in Switzerland. These authors only considered pig liver products, such as cold smoked liver sausage, or liver pâté, due to lack of data regarding other products. HEV prevalence in pig liver was estimated at 1.3% for Switzerland, compared to 6.6% in our study (Table 7). HEV gc present in the contaminated products ranging from 1.9 to 3.5 log gc/g, were consistent with our inputs of 2.1–3.8 log gc/g. In the study of Müller et al. (2017), mixing was considered, leading to a larger fraction of contaminated products, but at a reduced number of gc per gram due to dilution with other noncontaminated products, a step not considered in our current study. Second, in Müller et al. (2017) heating at 68–71°C for 5 min was considered to reduce virus infectivity (in gc) between 2.3 and 2.9 log gc/g. They assumed that 1% of HEV RNA was infectious in high-risk products, sold raw and inadequately cooked (Müller et al., 2017). Our study considered a reduction between 0.5 and 3.69 log gc/g for various ways of heating and/or storing based on results of a semiquantitative infectivity assay (Stunnenberg et al., 2023), a wider range than Müller et al. (2017). Müller et al. (2017) assumed that a product could potentially infect a consumer in case of HEV RNA levels above 105 gc per serving. For a probability of acute illness of 1% in our study, 4*105 gc per serving was needed. The probability of illness in our study is dependent on the viral load. A total of 176 cases were estimated for Switzerland, equivalent to 2 cases per 100,000 inhabitants (Müller et al., 2017), compared to 70 cases for the Netherlands, equivalent to 0.4 cases per 100,000 inhabitants (this study). The different assumptions and the different types of diets in both countries possibly lead to this large difference.

4.2 | Cost-effectiveness of the control measures

Control measures evaluated at the farm level led to a limited number of DALYs avoided per year. Vaccination led to the highest number of DALYs avoided (estimated at five per year for the Netherlands). All control measures lowered the transmission rate between pigs. This lower transmission rate resulted in a lower prevalence of contaminated livers at the end of the slaughtering stage: 4.3%, 4.8%, 5.2%, and 5.5% for the vaccination of finishing pigs, the use of rubber mats, the use of predatory flies, and the cleaning of the driving board, respectively, compared to 6.6% for the baseline scenario. Even though there was a decrease, the absolute decrease was limited. The most effective control measure against HEV was the proper heating of all pig meat and liver products before consumption. Fully heating products to at least 71°C for at least 5 min reduces significantly infectious HEV particles by 3.69 log (Stunnenberg et al., 2023). Proper heating will not eliminate all DALYs since, based on our model, unheated dried sausages, such as salami, are responsible for 67% of the expected DALYs.

The costs of the control measures ranged from €0.39 per pig for the cleaning of driving boards to €7.26 per pig for the vaccination of finishing pigs. This is a substantial increase in the cost of production since the current average animal health costs approximately €1.00 per finishing pig (Blanken

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et al., 2022). At the national level, the total costs ranged from €1 million for the cleaning of driving boards to €37 million for the vaccination of pigs. The costs per avoided DALY ranged from €0.52 to €7.49 million for the baseline scenario and could be lowered to between €0.52 and €5.35 million in case it was assumed that 90% of pig meat consumed in the Netherlands originated from domestically produced pigs. Comparing these costs to the estimated cost-of-illness per year for HEV attributable to food in the Netherlands, which ranges from €0.5 to €0.8 million between 2017 and 2021, none of the control measures would be cost-effective. However, in case, these control measures would also be effective for other pathogens and diseases, such as *Salmonella* spp., *Escherichia coli*, or swine influenza viruses, these measures could become cost-effective. In addition, the benefits in other countries where pig meat and liver products are sold, are not accounted for in our study. More research is needed to explore this further. Furthermore, for the effectiveness estimated in this study to be reached, the implementation of control measures is needed on all farms. Before farmers implement any control measure, they must be aware of the problem, for example, the presence of HEV at their farm, be motivated, and be capable of solving it. Interventions to solve one or more of these behavioral barriers might be needed (van Wagenberg et al., 2020).

Eppink et al. (2021) investigated the effectiveness and costs of three interventions against *Toxoplasma gondii* (*T. gondii*) at Dutch pig farms. Neutering of cats, coverage of feed, and professional rodent control led to a reduction of *T. gondii* seroprevalence of 67%, 96%, and no significant reduction, respectively. The costs ranged from €600 to €5,300 per farm (Eppink et al., 2021), so from €2 to €17 million at the national level considering 3270 pig farms (Agrimatie, 2023a). Benincà et al. (2022) estimated the number of DALYs due to *T. gondii* in pig meat to be 530 in 2021, with a cost-of-illness of €5 million, leading to much lower costs per avoided DALY for *T. gondii* than for HEV.

Van der Gaag, Saatkamp, et al. (2004) estimated the net costs for a package of interventions against *Salmonella* spp. at different points along the pork supply chain: finishing stage, transportation stage, lairage, and slaughtering stage summing up to €5.51 for all stages, with €2.99 for the finishing stage. This would add up to approximately €28 million at the national level considering 5.16 million finishing pigs (Agrimatie, 2023a). Benincà et al. (2022) estimated the number of DALYs due to *Salmonella* spp. in pig meat to be 100 in 2021, with a cost-of-illness of €2 million, leading to potentially lower costs per avoided DALY than for HEV but much higher than for *T. gondii*.

4.3 | Limitations of the model

Although the model allows the comparison of various control measures, it does have some limitations. The first limitation of our model is the fact that it models a pig farm of 1000 pigs, based on the model described by Mu et al. (2024). Larger farms, and especially larger pens, might lead to more contacts leading to a higher probability of infection as shown by the sensitivity analysis. Furthermore, sows were assumed to be seropositive for HEV and to transmit antibodies to the piglets, leading to maternal immunity during the first weeks. This maternal immunity slowly decreases and has no effect anymore after 12 weeks. In some cases, however, it might be possible that piglets do not inherit maternal immunity and are susceptible to HEV in the first weeks already. This would lead to an infection earlier in life, and a larger degree of recovery at slaughter age.

Inputs were mostly collected from the literature. As far as possible, data applicable to the Dutch situation were used. Several of these input values are uncertain, such as the number of gc per gram or the infectious period, both inputs having a large influence on the results. Even though a range for most inputs is considered, the results per farm can differ. In addition, assumptions are made such as the portion size, or the percentage of liver products not properly heated at home. A larger portion size would possibly lead to a larger number of infectious particles consumed, leading to a higher probability of illness, and possibly a higher burden of disease. A lower percentage of liver products, not properly heated would lead to a lower burden of disease.

4.4 | Implications of the model

The model developed is the first simulating HEV in the pig supply chain from farm-to-fork. The estimated DALYs, using the assumptions made, are close to the DALYs estimated based on reported cases. As such, the model can be used by decision-makers or food business operators along the pig supply chain to make objective decisions on the control of HEV. The model can be used to identify the most cost-effective management options. It can be further extended to other (new) control measures to evaluate their effectiveness. As the model is based on a previously derived *Salmonella* model, it shows it is a robust model approach capable of predicting the prevalence of food pathogens along the supply chain. As such, it can be extended to other pathogens such as *E. coli* or *T. gondii* using pathogen-specific indicators. By adjusting the inputs, the same type of model could be used for other countries with similar production systems as well.

5 | CONCLUSION

The model developed in this study simulated HEV along the pig supply chain including several stages: the pig farm, transport, lairage, slaughtering, processing, and consumption. The model estimated the burden of disease due to HEV in pig meat and liver products in the Netherlands, in terms of cases and DALYs. Furthermore, the cost-effectiveness of several control measures at the pig farms was investigated: cleaning driving boards, using predatory flies, using rubber mats on the floor, or vaccinating finishing pigs. The most cost-effective

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measure in this case study for the Netherlands was the cleaning of the driving boards with a cost-effectiveness ratio of €0.5 million per DALY avoided. The other control measures had even higher CER up to €7.5 million per DALY avoided, making none of the control measures cost-effective unless the control measures are also effective against other pathogens or the benefits in other countries are also considered.

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APPENDIX A: INPUT DATA USED TO ESTIMATE THE CONTROL MEASURES' COSTS

Input	Value	Reference
General		
Number of animals (numbers/farm)	1000	Assumption
Labor costs farmer (€/hour)	29.75	Blanken et al. (2022)
Labor costs employee (€/hour)	21.30	Blanken et al. (2022)
Number of cycles (#/year)	3.22	Blanken et al. (2022)
Vaccination		
Vaccination frequency (times/pig/cycle)	2	Go et al. (2021), Ji et al. (2021)
Labor farmer (seconds/dose/pig)	9	Assumption (400 finishing pigs per hour with 2 people)
Labor employee (seconds/dose/pig)	9	Expert estimate (400 finishing pigs per hour with 2 people)
Vaccination costs (€/dose)	1	Waninge (2020)
Weekly cleaning of driving boards		
Number of cleaning boards on the farm (#)	5	Assumption
Frequency cleaning boards (#/year)	52	Assumption
Cleaning time (minutes/board)	3	Assumption
Water use (liter/board)	10	Assumption
Costs water (€/m^3)	0.78	Blanken et al. (2022)
Predatory flies		
Costs predatory flies (€/delivered pig)	0.70	Bloemberg-van der Hulst (2022)
Frequency of predatory flies application (time/year)	4	Roelofs et al. (1998); commercially available predatory flies
Labor predatory flies' application (hours/application)	0.5	Assumption
Rubber mats on the floor		
Floor surface (m^2/pig)	1	Blanken et al. (2022)
Fraction floor with rubber of floor space/pig (fraction)	0.33	Assumption
Rubber mat costs (€/m^2)	55	Commercially available rubber mats
Labor to install rubber floor (hours/farm)	16	Assumption
Depreciation period (years)	10	Blanken et al. (2022)
Interest (% of investment)	3.5	Blanken et al. (2022)
Maintenance costs (% of investment)	1.0	Blanken et al. (2022)

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APPENDIX B: DEFAULT METHOD ESTIMATION OF THE FRACTION OF PIG MEAT CONSUMED IN THE NETHERLANDS FROM DOMESTICALLY RAISED FINISHING PIGS IN 2022

The default method to estimate the fraction of pig meat consumed in the Netherlands stemming from domestically raised finishing pigs as proposed by Mangen et al. (2007) uses the following equation:

$$\text{Fraction} = \frac{\text{Net slaughter weight} - \text{Imported } \textit{weight}}{\text{Net slaughter weight}} \cdot \frac{\text{Net slaughter weight} - \text{Exported meat and products}}{\text{Domestic consumption}}$$

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In this, all variables are expressed in tons of slaughter weight. Agrimatie provides the value of these variables for 2023 (Agrimatie, 2024).

- Net slaughter weight = 1,570,000 tons slaughter weight
- Imported weight = imported meat + imported live finishing pigs (= 370,000 tons + 10,000 finishing pigs times 100 kg slaughter weight per finishing pig)
- Exported meat and products = 1,300,000 tons of slaughter weight
- Domestic consumption = 640,000 tons of slaughter weight

Entering these values in the equation results in a fraction of (1,570,000 – 371,000)/1,570,000 · (1,570,000 – 1,300,000)/640,000 = 0.32.

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